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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,725	02/03/2004	Donald L. Durden	1857-ARTI.0024US-CON-2	2297

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EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	
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05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/770,725	DURDEN, DONALD L.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *91-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *91-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/23/04, 6/19/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of arthritis and Fcγ in the reply filed on 3/2/2007 is acknowledged.

Claims 91-101 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 93-100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 93-95 are confusing as to what is meant by the phrase "further comprising the administration of" an inhibitor of PI-kinase in claim 93 and an AKT inhibitor in claim 95. The term "further" implies that an inhibitor of PI-kinase or an AKT inhibitor is administered to the patient who received a PTEN agonist in claim 91. However, PI3 kinase inhibitors and AKT inhibitors in claim 93 and 95 are PTEN agonists according to the instant specification at Paragraph [0013], which discloses as follows; "PTEN agonists, PI3 kinase inhibitors and/or AKT inhibitors are administered to patients to prevent or inhibit immunoreceptor signaling." If claims 93-95 further limit the nature of "PTEN agonist of claim 91 to be an inhibitor of PI-kinase, LY294002, and an AKT inhibitor respectively, then the claims should be drafted accordingly.

Claim 96 recites "immunoreceptor" and claim 99 recites "ITAM". The specification at Paragraph [0148] discloses, "Fc gamma receptor mediated phagocytosis is a model for immunoreceptor (ITAM) signaling". This disclosure appears to indicate that the limitation "immunoreceptor" and "ITAM" are the same entity, and it is not clear why two different terms are used for single entity. In addition, claim 99 is construed using the term "modulates", which is broader than the term "inhibits" in claim 96. It is not clear how claim 99 further limit claim 96.

It is not clear how the dependent claims 96-100 further limit the base claim 91. It is not clear whether the dependent claims further limit the types (i.e. different chemical structures) of the agonist being administered or the same agonist in the base claim is being administered to solve different problems (different diseases as in claim 92). The third possibility is that the limitations in claims 96-100 are the inherent function of a PTEN agonist, as the specification at Fig. 12 seems to indicate. Note that disclosure that over-expression "of PTEN in COS7 cells inhibits ITAM signaling". This disclosure indicates that the function recited in claims 96-100 is the inherent function of a PTEN agonist".

For the purpose of this Office action, the Office will treat that "immunoreceptor" and "ITAM" refer to the same entity and the recited function in claims 96-100 is the inherent function of a PTEN agonist, and claims 93-95 further limit the agonist of the base claim 91 to be PI kinase, LY294002, and an AKT inhibitor in claims 93-95 respectively. However, this treatment does not relieve applicant the burden of responding to this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 91-93, 95, 96-101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 91-93, 95, 96-101 are drawn to a method using a genus of PTEN agonists, PI3 kinase inhibitors, AKT inhibitors.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a function of the genus. There is not even identification of any particular portion of a structure(s) that must be conserved in order to have the

recited function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). The specification at pages 44-45 discloses that the genus of PTEN agonist could be screened using the peptides listed at Table 1. The specification provides evidence for two art-known species, i.e. LY294002 and Wortmannin for the claimed genus. One species of ATK inhibitors is known in the art (see below the art rejection). Based on these three art-known species, one cannot predict the types of PTEN agonists, PI3 kinase inhibitors, AKT inhibitors. Since the genus includes a large number of unpredictable species, possession of only three species is not seen as sufficient to reasonably convey possession of the entire genus. It is concluded that applicants adequately describes the three art-known species. As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of PTEN agonists, PI3 kinase inhibitors, AKT inhibitors, given that the specification has only described LY294002 and Wortmannin. Therefore, only LY294002 and Wortmannin, but not

the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 91-100 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Pat. 6,632,789 (the '789 patent hereinafter, filing date of 4/1994).

Claims 91-100 are drawn to preventing or inhibiting inflammatory disease (claim 91) being arthritis (the elected species in claim 92) comprising administering a PTEN agonist (claim 91), an inhibitor of PI-kinase (claim 93), LY294002 (claim 94), an AKT inhibitor (claim 95), wherein claims 96-100 specify what the in vivo biological activity of the administered PTEN.

The '789 patent teaches at claims 1-19 a method of administering LY294002 (claim 1), PI-kinase inhibitor (claim 8), herbimycin A (claim 10), and Wortmannin (claim 16) for the purpose of ~~an effective amount of~~ my inhibiting a response by a T-cell. my 5-24-07

The '789 patent at Paragraph 12 and 13 teaches:

> To induce T cell unresponsiveness to an antigen in vivo, an agent, which inhibits production of D-3 phosphoinositides in a T cell, is administered to a subject at a dose and for a period of time sufficient to induce T cell unresponsiveness to the antigen. Following administration of the agent, antigen-specific T cells are contacted with the antigen endogenously (for example, an autoantigen expressed by cells endogenously). Alternatively, to induce T cell unresponsiveness to an antigen in vitro. In this case, T cells are obtained from a subject, contacted in vitro with the antigen together with the agent to induce antigenic unresponsiveness, and then readministered to the subject. For example, T cells obtained from a transplant recipient can be contacted with allogeneic cells from a graft donor together with an agent which inhibits D-3 phosphoinositide production in the T cells (e.g., wortmannin, quercetin, LY294002) prior to transplantation of the graft into the recipient to induce alloantigen-specific T cell unresponsiveness. The recipient T cells which have been rendered unresponsive to the donor antigens are then readministered to the recipient. Alternatively, in the case of bone marrow transplantation, bone marrow to be transplanted (including any residual T cells) can be contacted in vitro with allogeneic cells from the bone marrow recipient together with an agent which inhibits D-3 phosphoinositide production to induce unresponsiveness in the donor T cells to recipient alloantigens. This pretreatment can be performed to inhibit graft versus host disease.
>
> The methods for inducing T cell unresponsiveness can be applied therapeutically in situations where it is desirable to downmodulate an immune response, such as transplantation, including organ transplants and bone marrow transplants (as discussed above), and autoimmune diseases and other disorders associated with an abnormal immune response. Examples of autoimmune diseases or disorders associated with an inappropriate or abnormal immune response include rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, allergies, contact dermatitis, psoriasis, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, multiple sclerosis, allergic encephalomyelitis, systemic lupus erythematosus, acute necrotizing hemorrhagic encephalopathy, idiopathic bilateral progressive sensorineural hearing loss, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, polychondritis, scleroderma, Wegener's granulomatosis, chronic active hepatitis, myasthenia gravis, Stevens-Johnson syndrome, idiopathic sprue, lichen planus, Crohn's disease, Graves ophthalmopathy, sarcoidosis, primary biliary cirrhosis, primary juvenile diabetes, dry eye associated with Sjogren's syndrome, uveitis posterior, and interstitial lung fibrosis.

Since the instant specification at Paragraph [0013] discloses PI3 kinase inhibitors and/or AKT inhibitors are PTEN agonists being administered to patients to prevent or inhibit immunoreceptor signaling, the methods of administering LY294002 and Wortmannin, anticipates the claims, given that the '789 patent teaching at Paragraph 13 that arthritis is being treated by inducing T cell unresponsiveness.

As for claim 95 drawn to method of using an AKT inhibitor, Pendaries et al., The EMBO J., 2006, vol. 25, pages 1024-1034, at page 1030, left column, provide evidence that herbimycin A in claim 10 of the '789 patent meet the limitation of "an ATK inhibitor" in the instant claim 95. Note the disclosure that herbimycin A "strongly inhibited Akt phosphrylation".

Claims 91-93 and 96-101 are rejected under 35 U.S.C. **102(b)** as being anticipated by Schultz et al Anticancer Res. 1995 Jul-Aug;15(4):1135-9.

Claims 91-93 and 96-101 are drawn to preventing a inflammatory disease (claim 91) being arthritis (the elected species in claim 92) comprising administering a PTEN agonist (claim 91), an inhibitor of PI-kinase (claim 93), wherein claims 96-100 specify the different biological activities of the administered PTEN in vivo, and claim 101 specifies the route of the administration (oral, etc).

Schultz et al., teach (at Table VI) a method of administering Wortmannin orally to a patient. Since the instant claim 91 says that any PTEN agonist is able to prevent arthritis, Schultz et al's method inherently prevented arthritis in the in vivo subject.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 91-94 and 96-100 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,777,439. Although the conflicting claims are not identical, they are not patentably distinct from each other because the products being administered claims 1-3 of U.S. Patent No. 6,777,439 are species of the genus "PTEN agonist" claimed in the instant claims 91-94 and 96-100. The patent claims are not about inhibiting inflammatory disease. However, since the instant invention also includes preventing, the administered PTEN agonist in claims 1-3 of the patent would inherently prevent inflammatory disease. The claims of the patent have additional step of assessing angiogenesis. However, the instant claims construed with the open transitional phrases "comprising" do not exclude the assessing step.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MISOOK YU, Ph.D.
Primary Examiner
Art Unit 1642